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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAO, MANJUNATH N	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/922,067	MACPHEE ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,26 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,26 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence error report.*

DETAILED ACTION

Claims 25-26, 28 are currently pending in this application.

Applicants' amendments and arguments filed on 9-25-03, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Specifically based on the claim amendments and arguments provided by the applicants, Examiner has withdrawn the rejections under 35 U.S.C. 112, 2nd paragraph. Similarly, as applicants have now limited claim 25 to a human source, Examiner has withdrawn the rejection of claim 25 under 35 U.S.C. 112, Ist paragraph. Examiner has also withdrawn the rejection under Double Patenting rules as applicants have filed a TD.

Sequence Compliance

An error has been detected in the electronic sequence information submitted on 9-25-03, because of which the sequence information has not been entered into the USPTO sequence database. Applicant's attention is also drawn to the Sequence Error report enclosed herewith. See particularly 37 CFR 1.821(d).

Terminal Disclaimer

The terminal disclaimer filed on 9-25-03 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of 5,981,252 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 25, 26 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In response to the previous Office action, applicants have amended claim 25 and 28 with the recitation of the phrase "naturally occurring human". Applicants also indicate support for such amendment can be found on page 12, example 4 of the specification. However, a perusal of page 12 indicates the purification of the enzyme from LDL obtained from "plasma" followed by determination of the enzyme sequence. However, no where on the page is an indication that the plasma was from a human source. Therefore, the source of the enzyme cannot be concluded as that from human and above claims have no support for the phrase "naturally occurring human". Applicants can overcome the above rejection by canceling the phrase introduced into claim 25 and 28.

Claims 25, 26, 28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of polypeptides isolated from humans and at least 95% pure and having acetylhydrolase activity and comprising amino acids of SEQ ID NO:1, 2, 4, 10 or amino acids encoded by fragments of SEQ ID NO:9 such as nucleotides 929-1018. The specification does not contain any disclosure of the full structure of polypeptide sequences included in the claimed genera. The genus of polypeptides claimed is a large variable genus with the potentiality of having many different structures. Therefore, many structurally distinct polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus (i.e., the full length polypeptide encoded by SEQ ID NO:9) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. A sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by full sequence or a recitation of structural features common to members of the genus, **which features constitute a substantial portion of the genus**. The recited structural feature of the genus (i.e., polypeptides comprising fragments such as SEQ ID NO:1, 2, or 10) does not constitute a substantial portion of the genus as the remainder of the structure of any polypeptide having the above activity is completely undefined and the specification does not define the remaining structural features necessary for members of the genus to be selected. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous rejection, applicants have traversed the above rejection. Applicants argue that a "patent need not teach and preferably omits, what is well known in the art". Applicants also argue that Examiner appears to require that applicants disclose all possible amino acid sequences recited in claims 26 and 28 and discuss an example. Examiner respectfully disagrees with applicant's argument. Examiner was indeed not making it a requirement that "all" sequences be disclosed. It is regretted that such a meaning was implied by the rejection. As applicants have pointed out, the claims recite a genus wherein each member possess the same functional characteristic. However, the structural characteristics recited in the claims are not enough to be representative of the whole genus. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of

skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species or partial features within the genus. In the instant case the claimed genera of the polypeptides include species which are widely variant in structure. The recited structural feature of the genus (i.e., polypeptides comprising fragments such as SEQ ID NO:1, 2, or 10) does not constitute a substantial portion of the genus as the remainder of the structure of any polypeptide having the above activity is completely undefined and the specification does not define the remaining structural features necessary for members of the genus to be selected. The genus of above claims is structurally diverse (even when claimed from a single source, i.e., human) as it encompasses variants, mutants and recombinants. As such, the description of the structure provided is insufficient to be representative of the attributes and features of the entire genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed. Hence the above rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 25-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Steinbrecher et al. (J. Lipid Res., 1989, Vol. 30(3) :305-315) or Stremler KE et al. (J. Biol. Chem., 1989, Vol. 264(10):5331-5334). This rejection is based upon the public availability of printed publications. Claims 25-28 of the instant application are drawn to a lipoprotein associated phospholipase A2 that is at least 95% pure, wherein said enzyme is capable of hydrolyzing the sn-2 ester of a modified phosphatidylcholine, wherein said polypeptide has a molecular weight of 45-50 kDa, and comprises amino acid sequence of SEQ ID NO:1, 2, 4, 10 or 11, wherein said polypeptide is encoded by SEQ ID NO:9 or nucleotides 929-1018 of SEQ ID NO:9. It should be noted that said enzyme is also called as PAF-acetylhydrolase in the art. Stremler et al. and Steinbrecher et al. disclose an identical enzyme called as PAF-acetylhydrolase with characteristics identical to that claimed here (i.e., identical source, activity and molecular weight). However, the references do not provide the amino acid sequence or the nucleotide sequence encoding said enzyme. Based on the activity and the source of the enzyme, Examiner takes the position that a characteristic such as amino acid sequence is an inherent characteristic of any protein or enzyme and therefore the enzyme in the reference and the instant enzyme claimed are one and the same. Thus Steinbrecher et al. and Stremler et al. anticipate claims 25, 26, 28 as written.

Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

In response to the above rejection , applicants have traversed arguing that enzymes with similar activities and derived from the same source can have varied amino acid sequences and provide examples of polymorphic changes that can occur in amino acid sequence. While Examiner acknowledges the above phenomenon, he respectfully disagrees with the applicant's argument that the two references cannot inherently anticipate the claims, because there is an equal possibility that the proteins of the reference have the same amino acid sequence as claimed or at least comprise the sequence of fragments claimed in claim 26. Unless there is a compelling evidence (for example, a publication by the same authors providing the amino acid sequence of their respective enzymes that does not comprise the peptide sequences claimed herein or differs entirely from the polypeptide encoded by the full length of SEQ ID NO:9), Examiner continues to maintain his position that the polypeptide claimed and the polypeptide in the reference are one and the same and inherently have the same amino acid sequence as that claimed in the instant claims. Hence the rejection is maintained.

Conclusion

None of the claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.

MANJUNATH RAO
PATENT EXAMINER

Manjunath N. Rao
December 12, 2003